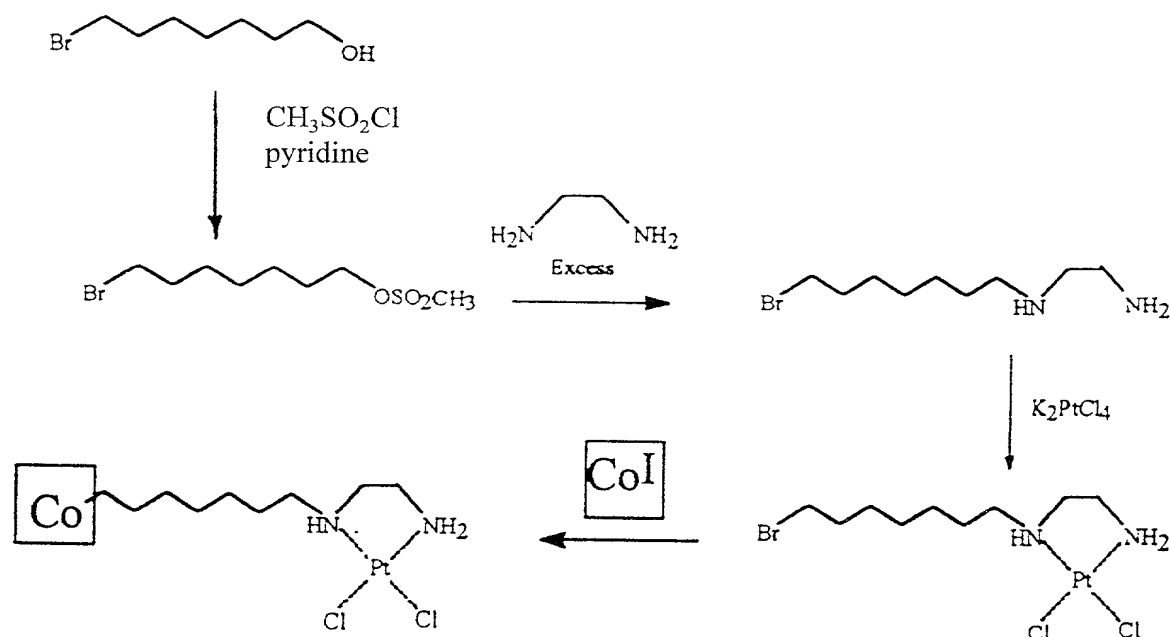


A carboplatin containing bioconjugate can be synthesized as shown in the following reaction scheme.



A peptide-containing bioconjugate can be synthesized by the following methods: (1) The C-terminal carboxyl group of the peptide can be activated and used to acylate Co(I), in analogy to the acylation of Co with chlorambucil acid chloride. (2) The C-terminal carboxyl group can be esterified with bromoethanol, in analogy to the other chlorambucil route, and the bromide displaced with Co(I). (3) The N-terminal amino group of the peptide can be treated with  $\text{CH}_2=\text{O}$  and Co(I) to form a Co(III)-  $\text{CH}_2\text{-NH-peptide}$  linkage, in analogy to the synthesis of the topotecan bioconjugate. (4) A Co(III)-amino acid complex can be prepared, and used in a coupling step with the remainder of the peptide. These methods can involve attachment of the Co at either the N- or C-terminus, or via a side-chain. A longer linker may be employed in any of these routes, if it is desirable to keep the cobalt complex further removed from the peptide chain.

